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VEGA *et al.*
PRELIMINARY AMENDMENT

acid molecules with a mutation at position 630 or within 1, 2, 3 . . . 10 or more bases thereof for the intracellular expression rep proteins or the rep gene mutants covered by claims 10 to 13, for the production of AAV or rAAV (either *in vitro*, *in vivo* or *ex vivo*) are provided. *In vitro* methods include cell free systems, expression or replication and/or virus assembly.

IN THE CLAIMS:

Please replace claims 6, 9, 24, 31, 33, 34 and 39 with the following amended claims (a marked up copy of the amended claims is attached to this Amendment):

6. (Amended) A mutant adeno-associate virus (AAV) Rep protein, comprising mutations at one or more of residues 4, 20, 22, 29, 32, 38, 39, 54, 59, 124, 125, 127, 132, 140, 161, 163, 193, 196, 197, 221, 228, 231, 234, 258, 260, 263, 264, 334, 335, 337, 342, 347, 350, 354, 363, 364, 367, 370, 376, 381, 389, 407, 411, 414, 420, 421, 422, 424, 428, 438, 440, 451, 460, 462, 484, 488, 495, 497, 498, 499, 503, 511, 512, 516, 517, 518, 542, 548, 598, 600 and 601 of AAV-2 or the corresponding residues in other serotypes, wherein residue 1 corresponds to residue 1 of the Rep78 protein encoded by nucleotides 321-323 of the AAV-2 genome, wherein the mutations comprise insertions, deletions or replacements of the native amino acid residue(s).

9. (Amended) A mutant AAV Rep protein of claim 6 that has increased activity compared to the native protein, wherein activity is assessed by measuring viral production when an AAV that encodes the protein is introduced into a cell under conditions wherein the virus replicates.

24. (Amended) The method of claim 23, wherein the AAV replicates.

31. (Amended) The method of claim 30, wherein the AAV replicates.

33. (Amended) A method of titering virus by a method designated tagged replication and expression enhancement, comprising:

(i) incubating host cells with a reporter virus vector and with a titering virus of unknown titer, wherein a titering virus increases or decreases the output signal from the reporter virus; and

(ii) measuring the output signal of the reporter virus and determining the titer of the reporter virus; and

(ii) determining the titer of the titering virus by comparing the titer of the reporter virus in the presence and absence of the titering virus.

34. (Amended) A process for the production of an adeno-associated virus (AAV) protein or a recombinant AAV having a predetermined property, comprising:

(a) producing a population of sets of nucleic acid molecules that encode modified forms of a target protein;

(b) introducing each set of nucleic acid molecules into host cells and expressing the encoded protein, wherein the host cells are present in an addressable array;

(c) individually screening each set of encoded proteins to identify one or more proteins that have activity that differs from the target protein, wherein each such protein is designated a hit;

(d) modifying the nucleic acid molecules that encode the hits, to produce a set of nucleic acid molecules that encode modified hits, wherein the nucleic acid molecules comprise rAAV vectors;

(e) introducing the each set of nucleic acids that encode the modified hits into cells; and

(f) individually screening the sets of cells that contain the nucleic acid molecules that encode the modified hits to identify one or more cells that